

Amendments to the Specification

Please insert on page 1 before the Background of the Invention section the following paragraph:

GOVERNMENT SUPPORT

The invention was supported in whole or in part, by a grant NIH RO1 NS33123-01A2 from the National Institutes of Health (NIH). The Government has certain rights in the invention.

Please replace the paragraph at page 1, lines 4 through 9 with the following amended paragraph:

This application is a continuation application of U.S. Application No. 09/083,268, filed May 22, 1998, now U.S. Patent No. 6,673,535, issued January 6, 2004, which is a divisional of U.S. Patent Application No. 08/727,084, filed October 8, 1996, now abandoned, which claims the benefit of U.S. Provisional Application No. 60/017,388, filed May 8, 1996, now abandoned, and U.S. Provisional Application No. 60/022,207, filed July 19, 1996, now abandoned. The entire teachings of the above applications are incorporated herein by reference.

Please replace the paragraph at page 6, lines 14 through 21 with the following amended paragraph:

The present invention provides isolated nucleic acids encoding the human SCA2 protein and isolated proteins encoded thereby. Further provided are vectors containing invention nucleic acids, probes that hybridize thereto, host cells transformed therewith, antisense oligonucleotides thereto and compositions containing, antibodies that specifically bind to invention polypeptides and compositions containing, as well as transgenic non-human mammals that express the invention protein. In addition, methods for diagnosing spinocerebellar Ataxia Type 2, or a ~~presisposition~~ predisposition thereto, are provided.

Please replace the paragraph at page 8, lines 1 through 6 with the following amended paragraph:

Figure 6 shows the composite cDNA sequence (SEQ ID NO:2) obtained from assembly of the partially overlapping cDNA clones shown in Figure 5. The predicted SCA2 protein product (SEQ ID NO:3) is shown below the DNA sequence. The stop codon for the SCA2 cDNA is indicated by *. The locations of primers SCA2-A (SEQ ID NO:6), SCA2-B (SEQ ID NO:7), and SCA2-B14 (SEQ ID NO:15) are indicated by horizontal arrows. The splice site between primers SCA2-B (SEQ ID NO:7) and SCA2-B14 (SEQ ID NO:15) is indicated by a vertical arrow.

Please replace the paragraph at page 37, line 26 through page 38, line 2 with the following amended paragraph:

Eighty ng each of primers SCA2-A (5'-GGG CCC CTC ACC ATG TCG-3') (SEQ ID NO:6) and SCA2-B (5'-CGG GCT TGC GGA CAT TGG-3') (SEQ ID NO:7) were added to 20 ng of human DNA with standard PCR buffer and nucleotide concentrations. After an initial denaturation at 95°C for 5 minutes, 35 cycles were repeated with denaturation at 96°C for 1.5 minutes, an annealing temperature of 63°C for 30 seconds, extension at 72°C for 1.5 minutes, and a final extension of 5 minutes at 72°C.

Please replace the paragraph at page 39, line 19 through page 40, line 2 with the following amended paragraph:

cDNA library screen: 32P-labeled probes were generated by PCR amplification of plasmid P65I22B using the following primer pair: 65A3: 5=CCGCGGCTGCCAATGTCC (SEQ ID NO: 8), 65B5: 5=GTAACCGTTCGGCGCCCG (SEQ ID NO: 9). A second probe was generated using primers 65A6: 5=GGCTCCCGGCGGCTCCTT (SEQ ID NO: 10); 65B6: 5=TGCTGCTGCTGCTGGGGCTTCAG (SEQ ID NO: 11). Screening of the trisomy 21 fetal brain cDNA library and the Stratagene adult human frontal cortex cDNA Lambda Zap II library

was performed using the amplification products generated from plasmid P65I22B. Phages were plated to an average density of 1×10^5 per 150 cm² plate. Plaque lifts of 20 plates (2×10^6 phages) were made using duplicated nylon membranes (Duralose-UV, Stratagene). Hybridization and excision were performed according to the manufacturer's protocol. Hybridized membranes were washed to a final stringency of 0.2x SSC, 0.1x SDS at 65°C. The filters were exposed overnight onto X-ray film. Excised phagemids were grown overnight in 5ml LB medium containing 50 ug/ml of ampicillin.

Please replace the paragraph at page 40, lines 17 through 25 with the following amended paragraph:

To obtain cDNA sequence for the 5' end of the SCA2 coding region, placental poly-T selected placental mRNAs (Clontech) were transcribed with MMLV reverse transcriptase and amplified with the following primer pairs: SCA2-A30: 5'CCGCCCCGCTCCTCACGTGT (SEQ ID NO: 12), SCA2-A31: 5'ACCCCCGAGAAAGCAACC (SEQ ID NO: 13); SCA2-B30: 5'-CCGTTGCCGTTGCTACCA (SEQ ID NO: 14). The sequences for primers SCA2-A30 and A31 were obtained from genomic sequence, and are located 5' to the stop codon preceding the putative initiator methionine. The sequence for SCA2-B30 was obtained from the 5' end of cDNA clones F1.1 and F1.2. The amplicons obtained by RT-PCR were directly sequenced.

Please replace the paragraph at page 41, line 28 through page 42, line 4 with the following amended paragraph:

RNA isolation and reverse transcription was carried out using well-known methods (Huynh et al., 1994, *Hum. Mol. Genet.*, 3:1075-1079). RNAs were isolated from lymphoblastoid cell lines established from patients and unrelated spouses in the FS pedigree with SCA2 (Pulst et al., 1993, *Nat. Genet.*, 5:8-10). Multiple tissue Northern blots were purchased from Clontech. For amplification, primers located in two exons (SCA-A and SCA-B14, see also Figure 6) were chosen so that genomic DNA was not amplified. The sequence for SCA-B14 was: 5'TTCTCATGTGCGGCATCAAG (SEQ ID NO: 15).